D2 Cont

14. (Twice Amended) The composition according to claim 2, wherein said nerve growth factor has a concentration of 0.1 to about 2.0 mg/ml.

D3 Sub E1

18. (Twice Amended) A composition produced by the process comprising formulating nerve growth factor (NGF) at a concentration from 0.07 to 20 mg/ml and a pharmaceutically acceptable acetate-containing buffer, wherein the buffer contains an acetate ion concentration of between 5 and 30 mM, and wherein the composition is of therapeutic purity and adapted for administration to humans.

REMARKS

Applicant respectfully requests the Examiner to reconsider the above-captioned application in view of the foregoing amendments and the following comments. As a result of the amendments listed above, Claims 2-5 and 7-21 are pending, Claims 2, 13, 14, and 18 have been amended, and Claim 6 has been canceled. The specific changes to the specification and the amended claims are shown on a separate set of pages attached hereto and entitled VERSION WITH MARKINGS TO SHOW CHANGES MADE, which follows the signature page of this Amendment. On this set of pages, the insertions are underlined while the ~~deletions are stricken through~~.

No new matter was introduced by way the amendments illustrated above. The amendments are fully supported by the specification, as discussed in detail below.

Claims 2-21 are definite.

Claim 2 has been amended to recite a particular NGF concentration range affirmatively disclosed in the specification at page 6, line 18. Claim 13 has been amended to remove the word "about." Notwithstanding these amendments, Applicants intend the scope of Claim 13 to encompass the stated concentration of NGF as well as the full range of equivalents to which they are entitled. Additionally, the pending claims have been amended to specify a range of acetate ion concentrations affirmatively disclosed at page 6, lines 8-9. This amendment serves to better distinguish the claimed subject matter from the prior art.

The pending claims are novel and nonobvious.

The pending claims are novel and nonobvious in part by inclusion of the term "pharmaceutically acceptable buffer.". The term "pharmaceutically acceptable buffer" is defined

by the specification to indicate a level of purity that would distinguish the claimed subject matter from the prior art. For example, the specification makes clear that the NGF containing compositions taught therein are intended for use in the treatment of mammals, preferably humans. Spec. at page 2, line 5. Moreover, the specification clearly contemplates the preparation of therapeutic formulations of NGF for use in humans. Spec at page 14, line 12 to page 15 line 14. Based on these and other statements in the specification, it is clear that the specification defines the term "pharmaceutically acceptable" to mean a solution that is suitable for administration as a pharmaceutical composition. Inherent in this definition are levels of purity, sterility, pH, absence of toxins, and other criteria that are notoriously well known to those of ordinary skill in the pharmaceutical arts.

Notwithstanding the implied level of purity present in the term "pharmaceutically acceptable," Applicants have amended independent Claims 2 and 18 to further recite that the claimed compositions are of a "therapeutic purity and adapted for administration to humans." By adding this limitation it should be clear to the Examiner that the claimed compositions are of a purity level suitable for use in humans. The prior art of record does not teach or suggest this level of purity. Thus, the subject matter of the pending claims is not anticipated by the cited art. Moreover, the pending claims are not obvious over the prior art of record, because none of the references provide a suggestion to modify their teachings to provide an NGF composition of therapeutic purity that is adapted for administration to humans.

CONCLUSION

Applicants have endeavored to address all of the Examiner's concerns as expressed in the Advisory Action dated November 25, 2002. Accordingly, amendments to the claims, the reasons therefor, and arguments in support of the patentability of the pending claim set are presented above. Any claim amendments which are not specifically discussed in the above remarks are made in order to improve the clarity of claim language, to correct grammatical mistakes or ambiguities, and to otherwise improve the capacity of the claims to particularly and distinctly point out the invention to those of skill in the art. In light of the above amendments and remarks, reconsideration and withdrawal of the outstanding rejections is specifically requested. If the Examiner finds any remaining impediment to the prompt allowance of these claims that could be

clarified with a telephone conference, the Examiner is respectfully requested to initiate the same with the undersigned.

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 11-1410.

Respectfully submitted,

KNOBBE, MARTENS, OLSON & BEAR, LLP

Dated: 9 DEC 2002

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the Claims:

Please cancel Claim 6 without prejudice.

Please amend claims 2, 13, 14, and 18 as follows:

2. (Amended) A pharmaceutical composition comprising **[a pharmaceutically effective amount of]** a nerve growth factor (NGF) at a concentration ranging from 0.07 to 20 mg/ml and a pharmaceutically acceptable acetate-containing buffer, wherein the buffer contains an acetate ion concentration of between 5 and 30 mM, and wherein the pharmaceutical composition is of therapeutic purity, adapted for administration to humans.

13. (Twice Amended) The composition according to claim 2, wherein the nerve growth factor has a concentration of at least **[about]** 0.1 mg/ml **[and said acetate-containing buffer comprises an acetate ion having a concentration of 10 mM to 50 mM]**.

14. (Twice Amended) The composition according to claim 2, wherein said nerve growth factor has a concentration of 0.1 to about 2.0 mg/ml **[and said acetate-containing buffer comprises an acetate ion having a concentration of 10 mM to 50 mM]**.

18. (Amended) A composition produced by the process comprising formulating nerve growth factor (NGF) at a concentration from 0.07 to 20 mg/ml and a pharmaceutically acceptable acetate-containing buffer, wherein the buffer contains an acetate ion concentration of between 5 and 30 mM, and wherein the composition is of therapeutic purity and adapted for administration to humans.